UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,319	03/09/2001	Daniel G. Anderson	0492611-0392 (MIT-9128)	5731

24280 7590 12/19/2005

CHOATE, HALL & STEWART LLP
TWO INTERNATIONAL PLACE
BOSTON, MA 02110

EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/803,319	ANDERSON ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *7,12-14,21-56 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-11, 15-20 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-58 are pending. Claims 7, 12-14, 21-56 and 58 are withdrawn from consideration. Claims 1-6, 8-11, 15-20 and 57 are examined.

Withdrawn Rejections

2. The rejection of Claims 2-5, 9-11, 15 and 16 under 35 U.S.C. 102(e) as being anticipated by Johnson et al., US 6,372,813 (IDS filed 12/06/2004), is withdrawn in view of applicant's arguments and amendments to the claims.

Priority

3. The instant application was filed 3/9/2001.

Declaration Under 37 CFR 1.131

4. The declaration (hereinafter Declaration) filed on 8/22/2005 under 37 CFR 1.131 has been considered but is ineffective to overcome the Kim et al. US 6,699,665. reference.

The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Kim et al., US 6,699,665 reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and

their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). The evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Kim et al., US 6,699,665 reference.

The Declaration does not clearly explain how Exhibit 1, i.e., the copy of several pages from the computerized laboratory notebook of Daniel Anderson, support the asserted facts, and does not explain where or how each claimed feature is shown, (which the examiner respectfully submits is not apparent). The examiner respectfully submits that the missing features would not have been obvious to the skilled artisan at the time.

In paragraph 4 of the Declaration, declarants state that Exhibit 1 provides evidence of conception and actual reduction to practice of the claimed invention prior to Nov. 8, 2000. In that paragraph, declarants state: "In particular, the pages describe the deposition of polymer elements on substrates coated with various material, including polyHEMA, and the culturing of cells on the polymer elements." This is complete extent of the declarants' explanation of how Exhibit 1 supports their assertion that the claimed invention was conceived and reduced to practice before No. 8, 2000.

Independent claim 1 recites:

> 1. A microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface; and a plurality of discrete dry polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers.

Newly amended independent claim 2 recites:

> 2. A microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface; and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers.

The Declaration does not indicate which substances coat the substrates, (and on which the polymer elements are alleged to be deposited) and does not indicate which substances are cytophobic, as in the claims. The aforementioned statement found in paragraph 4 of the Declaration indicates that "polyHEMA" is included among the substances described; and the specification, e.g., claim 6, indicates that poly(2-hydroxy-ethyl methacrylate) is a hydrogel that is comprised within a cytophobic surface. However, polyHEMA seems to appear only in one passage in Exhibit 1. Exhibit 1 there states:

> **coating slides w/ polyHEMA and bis amine PEG**
>
> Dissolve approximately 1gm of Poly HEMA (p3932) in 100% ethanol. Doesn't dissolve well in either chloroform or DMF. Ethanol solution is slowly dissolving, so rotate overnight. Also, dissolve 100mg of PEG-2 (NH_2) and dissolve in 1 ml of DMF.
>
> Add one spot to an epoxy and Xenobind slide and incubate 1hr at room temp. *at the other end of the slide*, take enough HEMA in EtOH to coat and place on slide. Allow to incubate 1 hr at room temp then 1hr at 37C. Slides were washed with PBS twice, and then cells were added in a 15 cm dish.
>
> PEG didn't keep cells from growing

Exhibit 1, at pp. 10-11, (emphasis added).

The examiner respectfully submits that on its face, the Exhibit appears to disclose that a polymer (PEG) and a cytophobic substance (Poly HEMA) are deposited at *opposite ends* of an epoxy and Xenobind slide and bound to the substrate, not to each other. Exhibit 1 fails to disclose that anything should be bound to a cytophobic surface, let alone a polymeric biomaterial element, as recited in claims 1 and 2. Neither Exhibit 1, nor the Declaration, mentions the term "cytophobic". Exhibit 1 does not appear to demonstrate possession of a microarray of different polymers non-covalently bonded to a cytophobic substance, as claimed. The Declaration does not appear to demonstrate a nexus between Exhibit 1 and the elements and limitations of the claims. Therefore, the examiner respectfully submits that the Declaration is insufficient to establish applicant's conception or reduction to practice before the priority date of the prior art reference of Kim et al., US 6,699,665.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-5, 8-11 and 15-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Kim et al., US 6,699,665. This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements

includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers.

Kim et al., throughout the patent and especially at col. 4, line 58-col. 5, line 38, teach a microarray of polymeric biomaterials comprising a base (including metal, glass, polystyrene, and polycarbonate), and teach a cytophobic surface, wherein the base is polymethylacrylate, which absent evidence to the contrary, is a hydrogel, as in claim 5, (specification at col. 6, lines 24-49); and an array of biomolecules that include molecules having a specific reactivity toward a particular surface, the remainder of the molecule being typically a hydrocarbon chain, which can be hydrophobic, cytophobic, or biophobic and is generated onto an substrate as a self-assembled monolayer (col. 9, lines 4-40) by direct coupling or by micro-contact printing; and, at col. 15, lines 45-67, teach an array of biomolecules prepared from solution of proteins ("e.g., 100 different proteins from a library) using an ink-jet; and at col. 8, lines 3-23, teach reactions (including ionic interaction, binding events, hydrophobic interaction, hydrogen bond formation, etc.) of the biomolecules, (including proteins, nucleic acids or chemical entities) with a substrate (which reads on a plurality of discrete, dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface), wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as claimed). Kim et al. at col. 7, lines 29-33, teach polymeric biomaterial elements ranging from 1 micron to about 1 mm, (as in claims 15 and 16); and at col. 7, lines 13-18, teach intervals measuring 1 cm to about 0.5 cm to about 0.25 cm distances, (as in claims 17 and 18). Kim at col. 10, lines 19-28, teach over 2,000 array elements in the area of a standard well of a 96-well plate (approximately mm^2), which absent evidence to the contrary, read on claims 19 and 20, reciting limitation of 1 to 1000 or 10-100 polymeric biomaterial elements per cm^2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Kim et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

In regards to the limitation that the polymeric biomaterial elements include different soluble synthetic polymers, it is note that the specification does not disclose how synthetic polymers of poly(amino acids) differ from proteins, or proteins libraries. Absent evidence to the contrary, the proteins and protein libraries as taught by Kim et al. do not differ from synthetic polymers of poly(amino acids).

Applicant argues that in view of the Declaration under 37 CFR 1.131, the reference of Kim et al. does not qualify as prior art under 35 USC 102(e).

Response to Arguments

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. The examiner respectfully submits that the Declaration is insufficient, (see above section Declaration Under 37 CFR 1.131).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1-6, 8-11, 15-20, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Schultz et al., US 5,985,356**, (IDS filed 3/11/2003); **Sheu et al.**, (J. Adhesion Sci. Technol., 1992, Vol. 6, No. 9, pp. 995-1009); **Kapur et al., US 6,548,263**, (previously cited by examiner, 11/21/2003); and **Koob et al., US 20030204023**. This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Schultz et al. (US 5,985,356), throughout the patent, teach microarrays of polymeric biomaterials comprising: a base (including metals and glass) comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements that include polyurethanes, polycarbonates, polystyrene, (col. 7, lines 34-56; col. 11, line 41-col. 12, line 5; and as in instant claim 11) non-covalently bound to said surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers. Schultz et al., at col. 4, lines 30-46, teach that an array of materials on a single substrate can consist of more that 10, more than 100, more than 1000 materials, and so fourth. Schultz et al. at col. 33, lines 14-51, and Figure 9, teach synthesis of an array of 16 different organic polymers of styrene and acrylonitrile and initiator, wherein the monomers are delivered by ink-jet dispenser; upon completion of polymerization on the substrate, the organic solvent is removed by evaporation *in vacuo*, which reads upon dry polymeric biomaterial elements. Schultz et al., at col. 11, line 41-col. 12, line 5, teach arrays of diverse materials at known locations on a single substrate surface and teach that the substrates can be coated with a material different from the base, and state that "[t]he most appropriate substrate and substrate-surface materials will depend on the class of materials to be synthesized and the selection in any given case will be readily apparent to those of skill in the art." Schultz et al., at col. 15, lines 18-65, also teach thin-film deposition techniques. Schultz et al. at col. 12, lines 6-34, teach regions that are less than 1,000 μm^2 (as in claims 15 and 16). Schultz et al., at col. 23, lines 35-48, disclose that spacing between the individual regions will vary in accordance with the sized of the regions used, for example, if a 1 mm^2 region is used, the spacing will be on the order of 1 m or less. If a 10 μm^2 region is used, then the spacing will be on the order of 10 μm. Thus the intervals as claimed in claims 17 and 18 are within the ranges taught by Schultz et al. At col. 4, lines 30-47, Schultz et al. teach 1 to 10 to 100 to 1000 to 10,000

regions/cm^2, so that if one compound is polymerized on one region, then the density of polymeric biomaterial elements per cm^2 is encompasses the ranges claimed in claims 19 and 20.

Schultz et al. (US 5,985,356), does not disclose microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, wherein polymeric elements are bound to the cytophobic surface; and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug. Schultz et al. do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Sheu et al., (J. Adhesion Sci. Technol., 1992, Vol. 6, No. 9, pp. 995-1009), throughout the publication and especially in the abstract, p. 995, para 1-p. 996, para 1, teach non-fouling surfaces, including surfaces containing poly(ethylene glycol) (PEG) or poly(ethylene oxide) (PEO) that show high surface wettability and low affinity for proteins and cells. Sheu et al., at p. 998, teach dip-coating surfaces to deposit PEO surfactants.

Kapur et al., (US 6,548,263), throughout the patent, and especially at col. 41, line 43-col. 43, line 6, teach arrays of various sizes, rendering array surfaces repulsive for cellular adhesion, in order to pattern cell attachment and growth on a surface; and Kapur et al. teach using hydrogel as a cytophobic surface. Kapur et al., at, e.g., col. 18, line 60-col. 19, line 65, especially col. 19, line 48, teach that various cell binding, marker and other molecules can be used in the arrays, including "drugs".

Koob et al., US 20030204023, at para [0155] teach that poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, and polymeric elements that are bound to the cytophobic surface; wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate); and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, and wherein polymeric elements are bound to the cytophobic surface, in order to avoid following of substrates by protein and cells and to control the patterns of cell growth on substrates. Schultz et al. teach that the practitioner may select a substrate upon which to generate a polymeric array, depending upon the material to be synthesized; Sheu et al., teach that the synthesis of cytophobic surfaces coated with PEG or PEO so as to prevent fouling by proteins and cells; and Kapur et al. using multiple layers of cell adhesive and cell repulsive surfaces to control the pattern of cell growth on surface. One of ordinary skill in the art would have been motivated to make cytophobic surface that comprises poly(2-hydroxy-ethyl methacrylate) because Koob et al. teach poly(2-hydroxy-ethyl methacrylate) is cytophobic.

One of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of Schultz et al., Sheu et al., and Kapur et al., because Sheu et al. and Koob et al. taught cytophobic surfaces, including poly(2-hydroxy-ethyl methacrylate), were well known in the art at the time the invention was made; and because polymerization on substrates is taught by Schultz et al.

Applicant argues that the combination of the aforementioned prior art references would result in the disclosure of Kapur, in which cytophobic and cytophilic material are deposited side-by-side on a substrate, and not the invention recited in claims 1 and 2.

Response to Arguments

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, and wherein polymeric elements are bound to the cytophobic surface, in order to avoid following of substrates by protein and cells and to control the patterns of cell growth on substrates. Schultz et al. teach that the practitioner may select a substrate upon which to generate a polymeric array, depending upon the material to be synthesized; Sheu et al., teach that the synthesis of cytophobic surfaces coated with PEG or PEO so as to prevent fouling by proteins and cells; and Kapur et al. using multiple layers of cell adhesive and cell repulsive surfaces to control the pattern of cell growth on surface.

7. Claims 1-6, 8-11, and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Kim et al., US 6,699,665**; and **Koob et al., US 20030204023**. This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Kim et al., US 6,699,665, throughout the patent and especially at col. 4, line 58-col. 5, line 38, teach a microarray of polymeric biomaterials comprising a base (including metal, glass, polystyrene, and polycarbonate), and teach a cytophobic surface, wherein the base is polymethylacrylate, which absent evidence to the contrary, is a hydrogel, as in claim 5, (specification at col. 6, lines 24-49); and an array of biomolecules that include molecules having a specific reactivity toward a particular surface, the remainder of the molecule being typically a hydrocarbon chain, which can be hydrophobic, cytophobic, or biophobic

and is generated onto an substrate as a self-assembled monolayer (col. 9, lines 4-40) by direct coupling or by micro-contact printing; and, at col. 15, lines 45-67, teach an array of biomolecules prepared from solution of proteins ("e.g., 100 different proteins from a library) using an ink-jet; and at col. 8, lines 3-23, teach reactions (including ionic interaction, binding events, hydrophobic interaction, hydrogen bond formation, etc.) of the biomolecules, (including proteins, nucleic acids or chemical entities) with a substrate (which reads on a plurality of discrete, dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface), wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as claimed). Kim et al. at col. 7, lines 29-33, teach polymeric biomaterial elements ranging from 1 micron to about 1 mm, (as in claims 15 and 16); and at col. 7, lines 13-18, teach intervals measuring 1 cm to about 0.5 cm to about 0.25 cm distances, (as in claims 17 and 18). Kim at col. 10, lines 19-28, teach over 2,000 array elements in the area of a standard well of a 96-well plate (approximately mm^2), which absent evidence to the contrary, read on claims 19 and 20, reciting limitation of 1 to 1000 or 10-100 polymeric biomaterial elements per cm^2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Kim et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

In regards to the limitation that the polymeric biomaterial elements include different soluble synthetic polymers, it is note that the specification does not disclose how synthetic polymers of poly(amino acids) differ from proteins, peptides, polypeptide, or oligopeptides. Absent evidence to the contrary, the proteins and protein libraries as taught by Kim et al. do not differ from synthetic polymers of poly(amino acids).

Kim et al. do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Koob et al., US 20030204023, at para [0155] teach that poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate) because Koob et al., teach poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using cytophobic surfaces that comprise poly(2-hydroxy-ethyl methacrylate) because poly(2-hydroxy-ethyl methacrylate) is a hydrogel.

Applicant argues that in view of the Declaration under 37 CFR 1.131, the reference of Kim et al. does not qualify as prior art under 35 USC 102(e).

Response to Arguments

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. The examiner respectfully submits that the Declaration is insufficient, (see above section Declaration Under 37 CFR 1.131).

8. Claim 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Kim et al., US 6,699,665**; and **Kapur et al., US 6,548,263**, (previously cited by examiner, 11/21/2003). This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

Kim et al., US 6,699,665, throughout the patent and especially at col. 4, line 58-col. 5, line 38, teach a microarray of polymeric biomaterials comprising a base (including metal, glass, polystyrene, and polycarbonate), and teach a cytophobic surface, wherein the base is polymethylacrylate, which absent evidence to the contrary, is a hydrogel, as in claim 5, (specification at col. 6, lines 24-49); and an array of biomolecules that include molecules having a specific reactivity toward a particular surface, the remainder of the molecule being typically a hydrocarbon chain, which can be hydrophobic, cytophobic, or biophobic and is generated onto an substrate as a self-assembled monolayer (col. 9, lines 4-40) by direct coupling or by micro-contact printing; and, at col. 15, lines 45-67, teach an array of biomolecules prepared from solution of proteins ("e.g., 100 different proteins from a library) using an ink-jet; and at col. 8, lines 3-23, teach reactions (including ionic interaction, binding events, hydrophobic interaction, hydrogen bond formation, etc.) of the biomolecules, (including proteins, nucleic acids or chemical entities) with a substrate (which reads on a plurality of discrete, dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface), wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as claimed). Kim et al. at col. 7, lines 29-33, teach polymeric biomaterial elements ranging from 1 micron to about 1 mm, (as in claims 15 and 16); and at col. 7, lines 13-18, teach intervals measuring 1 cm to about 0.5 cm to about 0.25 cm distances, (as in claims 17 and 18). Kim at col. 10, lines 19-28, teach over 2,000 array elements in the area of a standard well of a 96-well plate (approximately mm^2), which absent evidence to the contrary, read on claims 19 and 20, reciting limitation of 1 to 1000 or 10-100 polymeric biomaterial elements per cm^2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by

process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Kim et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

In regards to the limitation that the polymeric biomaterial elements include different soluble synthetic polymers, it is note that the specification does not disclose how synthetic polymers of poly(amino acids) differ from proteins, peptides, polypeptide, or oligopeptides. Absent evidence to the contrary, the proteins and protein libraries as taught by Kim et al. do not differ from synthetic polymers of poly(amino acids).

Kim et al. do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

Kapur et al., US 6,548,263, at, e.g., col. 18, line 60-col. 19, line 65, especially col. 19, line 48, teach that various cell binding, marker and other molecules can be used in the arrays, including "drugs".

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug, because Kapur et al., teach testing and interacting cells with small drug molecules on arrays.

One of ordinary skill in the art would have had a reasonable expectation of success in making arrays that comprised small drug molecules, because the attachment of small organic molecules to polymers was well known in the art.

Applicant argues that in view of the Declaration under 37 CFR 1.131, the reference of Kim et al. does not qualify as prior art under 35 USC 102(e).

Response to Arguments

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. The examiner respectfully submits that the Declaration is insufficient, (see above section Declaration Under 37 CFR 1.131).

Conclusion

9. Claims 1-6, 8-11, 15-20 and 57 stand finally rejected. Claims 7, 12-14, 21-56 and 58 remain withdrawn from consideration.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms

PADMASHRI PONNALURI
PRIMARY EXAMINER